Remarks

The Examiner's Action addressed all of Applicants' then pending claims, namely Claims 1 to 16. Claims 11, 14 and 16 have been cancelled. Claims 1, 4, 7, 8, 12, 13 and 15 have been amended to delete non-elected subject matter. In view of the foregoing amendments and the following remarks, reconsideration and withdrawal of the rejections are respectfully requested.

Claims 1 to 16 have been objected to as containing non-elected subject matter. Applicants submit that the foregoing amendments to Claims 1, 4, 7, 8, 12, 13 and 15 have rendered this objection moot. Accordingly, withdrawal of the objection is respectfully requested.

Claims 11 and 12 have been rejected under 35 U.S.C. § 112, second paragraph, Claims 10 and 11 have been rejected under 35 U.S.C. § 112, first paragraph, and Claim 11 has been rejected under 35 U.S.C. § 101. Applicants submit respectfully that the rejections of Claim 11 are moot in view of the cancellation of same.

Discussion of the Rejections under 35 U.S.C. § 112, Second Paragraph

Claim 12 has been rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention as "steps (D)-(J) are confusing". The Examiner contends that it is unclear if optional steps (D) through (J) are meant to be consecutive or carried out as individual alternative steps. Applicants respectfully submit that this rejection is moot in view of the amendments to Claim 12.

The Examiner also contends that Claim 12 is allegedly indefinite as it is unclear how each step is conducted absent a recital of the reaction conditions, solvents, etc. Applicants note that the specification is to be interpreted in light of the knowledge of one of ordinary skill in the art. One of ordinary skill in the art would know how to convert the claimed compound into salt, non-salt, oxidized, non-

oxidized, etc. forms. Accordingly, this rejection is respectfully traversed as the lack of a recitation of such reaction conditions does not render Claim 12 indefinite.

Discussion of the Rejection under 35 U.S.C. § 112, First Paragraph

Claim 10 has been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement with regard to the use of the compounds of Claim 1 for the treatment of diseases. Applicants traverse this rejection as one skilled in the art, having read the present specification, would be able to make and use the present inventions without engaging in undue experimentation.

The first paragraph of § 112 requires that the disclosure of a patent application be such that persons skilled in the art, having read the patent application, would be able to practice the inventions defined by the claims. *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). There is no legal requirement that this be done in any particular manner. An enabling disclosure can be provided by the use of illustrative examples or simply by broad terminology. *In re Marzocchi*, 169 U.S.P.Q. 367 (C.C.P.A. 1971). The test of enablement is ***not*** simply whether experimentation would have been necessary, but whether such experimentation would have been ***undue***. *See In re Angstadt*, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *See Wands*, 8 U.S.P.Q.2d at 1404. The factors to be considered (hereinafter "the *Wands* factors") in determining whether any necessary experimentation is undue include:

i. the breadth of the claims;
ii. the nature of the invention;
iii. the state of the prior art;
iv. the level of one of ordinary skill;
v. the level of predictability in the art;
vi. the amount of direction provided by the inventor;

vii. the existence of working examples; and

viii. the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Id. (*citing Ex parte Forman*, 230 U.S.P.Q. 546, 547 (Bd. Pat. App. & Int. 1986)). Any conclusion of non-enablement must be based on the evidence as a whole. *Id.* Significantly, a patent application need not disclose what is well known in the art. *Id.*

When rejecting a claim under the enablement requirement of § 112, first paragraph, the Patent Office bears the "initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification." *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). To object to an applicants' disclosure on the grounds that it is not enabling with respect to the scope of a claim sought to be patented, the Action must identify evidence or technical reasoning supporting any doubts regarding applicants' enablement of the claim. *Id.*; and MPEP § 2164.04. Without a reason to doubt the truth of the statements made in the patent application, the application must be considered enabling. *In re Wright*, 27 U.S.P.Q.2d at 1513; *In re Marzocchi*, 169 U.S.P.Q. at 369.

Despite the Action's assertion that those skilled in the art would need to engage in undue experimentation to utilize the instant compounds to treat "all disorders responsive to the inhibition of Cathepsin S" (Action at 4-5), a review of the scientific literature reveals that there is no reason to believe that those of ordinary skill would have any difficulty in using the compounds of Claim 10 to treat, for example, the diseases recited in Applicants' claims or that, if experimentation ***were*** required, such experimentation would not be routine in nature. For the reasons detailed below, Applicants submit respectfully that consideration of the *Wands* factors demonstrate that those skilled in the art would be able to treat the claimed diseases without engaging in undue experimentation.

The Nature of the Invention

According to the Action, the nature of Applicants' invention is the "inhibition of Cathepsin S, comprising administering the instant claimed compound to a subject in need thereof" (Action at 5). The Action alleges that Claim 10 is in the form of a reach-through claim, drafted in terms of inhibiting a cellular event, and accordingly one skilled in the art would not know how to perform the claimed method (Action at 5). The Action has not provided any reason as to how or why this factor contributes to the alleged lack of enablement.

The Predictability in the Art

It is asserted in the Action that "one of skill in the art is unable to fully predict possible results from the administration of the claimed compounds" due to "the absence of a showing of correlation between all the diseases alleged as capable of being treated by the compound of the instant claims and the response of Cathepsin S activity" (Action at 5-6). The Action, however, provides no evidence or technical reasoning in support of such statement. Significantly, the Action appears to have overlooked a plethora of literature that shows the predictable relationship between the inhibition of Cathepsin S and the diseases recited in Applicants' claims. In this regard, Exhibit A (attached hereto) presents a summary of twenty-one (21) publications of which Applicants are aware (copies enclosed), which provides solid evidence that those of ordinary skill in the art have knowledge of the link between at least eighty-four (84) diseases and inhibition of Cathepsin S, that is, that there are at least 84 diseases which can be treated or prevented by inhibition of Cathepsin S. Accordingly, there is a low level of unpredictability regarding the instantly claimed invention.

The Presence or Absence of Working Examples
& the Amount of Direction or Guidance Present

The Action does not allege that the compounds of the present invention do not inhibit Cathepsin S (Action at 6). The Action, however, finds fault with the working examples because the compounds allegedly have not been tested for their ability to treat the full scope of disorders detailed in the specification; however, a patent need not teach, and preferably omits, what is well known in the art. MPEP § 2164.01. As detailed above, Exhibit A provides solid evidence that those of ordinary skill in the art have the knowledge and the link ability to identify diseases which are limited to inhibition of Cathepsin S. Thus, in view of Exhibit A submitted herewith, Applicants' working examples are sufficient to enable the claimed invention.

The Breadth of the Claims

Applicants submit that, for the reasons detailed above, the full breadth of the claims is enabled by Applicants' disclosure when considered in view of the knowledge in the art.

The Quantity of Experimentation Needed

The Action alleges that the quantity of experimentation needed is undue (Action at 7). This statement, however, is demonstrably not supported by the record. As detailed above, Applicants have provided 21 publications detailed in Exhibit A that demonstrate that those of ordinary skill in the art have knowledge of at least 84 diseases that would be benefited by inhibition of Cathepsin S. Accordingly, to the extent that any experimentation is required to practice the claimed invention (*arguendo*), such experimentation is far less than that alleged by the Action, is not undue, and for those skilled in the art, can be considered routine.

The Level of the Skill in the Art

Applicants agree with Examiner's statement that the level of skill in the art is

high (Action at 7). In view of such high level of skill and the knowledge that such high level entails (as evidenced by the 21 publications submitted herewith), Applicants submit that the present disclosure enables the full scope of the claims.

Thus, for all of the reasons detailed above, it is respectfully submitted that Applicants' claims are fully enabled by the present disclosure; one skilled in the art would not have to engage in undue experimentation to practice any of the claimed methods. Accordingly, reconsideration and withdrawal of the rejection are requested respectfully.

Conclusion

Applicants submit respectfully that this application is now in condition for allowance. Accordingly, an indication of allowability and an early Notice of Allowance are requested respectfully.

The Commissioner is authorized hereby to charge any fees or credit any overpayment associated with this Reply (copy enclosed) to Deposit Account Number 19-5425.

Respectfully submitted,

Date: January 12, 2006

Alexis Barron
Registration No. 22,702

Synnestvedt & Lechner LLP
2600 Aramark Tower
1101 Market Street
Philadelphia, PA 19107
Telephone (215) 923-4466
Facsimile (215) 923-2189

CMM
M:\CMcAvoy\sanofi-aventis\27872 Series\P27872-B USA - Reply to Action of 07.12.05 v2.doc

Exhibit A

No.	Publication Number	Title	Use
1	WO 2000051998	**New heteroaryl- or cyano-substituted peptide compounds, are reversible cathepsin S inhibitors useful for treating autoimmune diseases, Alzheimer's disease or atherosclerosis.**	inhibition of cathepsin for treating autoimmune diseases (specifically rheumatoid arthritis, systemic lupus erythematosus, Crohn's disease, ulcerative colitis, multiple sclerosis, Guillain-Barre syndrome, psoriasis, Graves disease, myasthenia gravis, scleroderma, glomerulonephritis, atopic dermatitis or insulin-dependent diabetes mellitus), Alzheimer's disease or atherosclerosis
2	WO 2000049008	**New di- and tripeptide nitrile derivatives, useful for treating cathepsin L or S mediated disease states, particularly chronic obstructive pulmonary disease.**	inhibition of cathepsin for treating bone resorption diseases such as osteoporosis, rheumatoid arthritis, osteoarthritis, tumor metastasis, pneumocystitis, Crithidia fusiculata, malaria, Trypanosoma brucei, schistosomiasis, periodontal disease, metachromatic leukodystrophy and muscular dystrophy.
3	WO 2000049007	**Acetamido acetonitrile derivatives, useful for the treatment of chronic obstructive pulmonary disease, are cathepsin L and/or S inhibitors.**	inhibition of cathepsin for treating chronic obstructive pulmonary disease
4	WO 2000048992	**New acylated aminoacetonitrile derivatives useful for treating cathepsin L or cathepsin S mediated diseases e.g. chronic obstructive pulmonary disease.**	inhibition of cathepsin for treating chronic obstructive pulmonary disease.

No.	Publication Number	Title	Use
5	WO 9808494	**Method for ameliorating symptoms of bone-resorption disorder(s) - comprises treating osteoclasts with inhibitor of cathepsin K, useful for, e.g. treating osteoporosis.**	inhibition of cathepsin for treating osteoporosis, osteoarthritis and periodontal disease, macrophage-mediated damage to bone, lungs, e.g. emphysema or at the site of atherosclerotic plaque, atherosclerotic disorders, (especially pycnodysostosis (PYCNO))
6	WO 9740066	**Suppressing immune and allergic responses - by administering agent which inhibits cathepsin S.**	inhibition of cathepsin for treating autoimmune diseases (especially juvenile-onset diabetes, multiple sclerosis, pemphigus vulgaris, Grave's disease, myasthenia gravis, systemic lupus erythematosus, rheumatoid arthritis or Hashimoto's thyroiditis), allergic responses (especially asthmatic responses) or organ or tissue transplant rejection
7	WO 2001019796	**New (sulfonyl substituted alkyl) cyanomethyl amide as cathepsin S inhibitors for treating e.g. autoimmune disorders, allergic disorders, allogenic immune responses and systemic amyloidosis.**	inhibition of cathepsin for treating for treating autoimmune disorders (such as juvenile onset diabetes, multiple sclerosis, pemphigus vulgaris, Graves' disease, myasthenia gravis, systemic lupus erythemotasus, rheumatoid arthritis, and Hashimoto's thyroiditis) allergic disorders (such as asthma), allogenic immune responses (such as organ transplant or tissue grafts), systemic amyloidosis, disorders involving excessive elastolysis (such as chronic obstructive pulmonary disease, bronchiolitis and excessive airway elastolysis in asthma

No.	Publication Number	Title	Use
8	WO 2001009169	New alpha-amino acid amide derivatives, are cysteine protease inhibitors, especially cathepsin inhibitors, useful in treatment of, e.g. osteoporosis, cardiac ischemia or muscular dystrophy.	inhibition of cathepsin for treating muscular dystrophy, osteoporosis, tumor metastasis, rheumatoid arthritis, neuronal or cardiac ischemia, allergic immune responses and protozoal or bacterial diseases.
9	WO 2000069855	New furanone derivatives which inhibit cathepsin S are useful for treatment of autoimmune diseases, multiple sclerosis allergies and rheumatoid arthritis.	inhibition of cathepsin for treating. autoimmune diseases, allergies, multiple sclerosis and rheumatoid arthritis.
10	WO 2000055126	New N-cyanomethylamides as cysteine protease inhibitors useful for treating e.g. osteoporosis in post menopausal women, tumor invasion and metastasis, rheumatoid arthritis or osteoarthritis.	inhibition of cathepsin for treating osteoporosis, tumor invasion and metastasis, rheumatoid arthritis, osteoarthritis, pneumocystis carinii, acute pancreatitis, inflammatory airway disease and asthma, auto-immune diseases (e.g. juvenile onset diabetes, multiple sclerosis, pemphigus vulgaris, Graves' diseases, myasthenia gravis, systemic lupus erythematosus, and Hashimoto's thyroiditis) and preventing the rejection of organ transplants.
11	WO 2000055125	N-Cyanomethyl-amide derivatives are cysteine protease inhibitors useful for treating e.g. asthma, tumor invasion and rheumatoid arthritis.	inhibition of cathepsin for treating asthma

No.	Publication Number	Title	Use
12	WO 2000055144	New amine derivatives as cysteine protease inhibitors useful for treating asthma, juvenile onset diabetes, multiple sclerosis, pemphigus vulgaris or Graves' disease.	inhibition of cathepsin for treating autoimmune disorder, allergic disorder, alogeneic immune response, a disorder involving excessive elastolysis, cardiovascular disorders or a disorder involving fibril formation, preferably juvenile onset diabetes, multiple sclerosis, pemphigus vulgaris, Graves' disease, myasthenia gravis, systemic lupus erythemotasus, rheumatoid arthritis, Hashimoto's thyroiditis, asthma, organ transplant, tissue graft rejections, chronic obstructive pulmonary disease, bronchiolitis, excessive airway elastolysis in asthma and bronchitis, plaque.
13	WO 2001055123	New tetrazole and oxadiazolone derivatives are cysteine protease inhibitors used for treating e.g. inflammatory, autoimmune, circulatory, neurodegenerative and pulmonary disorders.	inhibition of cathepsin for treating inflammatory diseases, diseases induced by apoptosis, diseases induced by immune response failure, autoimmune diseases, diseases induced by the degradation of biological constituting proteins, shock, circulatory disorders, blood coagulation system disorders, malignant tumor, AIDS, AIDS-related complex, parasitosis, neurodegenerative diseases, pulmonary disorders, bone resorption diseases and endocrine hyperenergia diseases including periodontal disease, arthritis, inflammatory bowel disease, myocarditis, spinal disorders, hepatitis C, liver cirrhosis, diabetes, reperfusion disorders, disseminated intravascular coagulation, Alzheimer's disease

No.	Publication Number	Title	Use
14	WO 2001044214	**New oxadiazole derivatives are cysteine protease inhibitors used for treating e.g. inflammatory, autoimmune, circulatory, neurodegenerative and pulmonary disorders.**	inhibition of cathepsin for treating inflammatory diseases, diseases induced by apoptosis, diseases induced by immune response failure, autoimmune diseases, diseases induced by the degradation of biological constituting proteins, shock, circulatory disorders, blood coagulation system disorders, malignant tumor, AIDS, AIDS-related complex, parasitosis, neurodegenerative diseases, pulmonary disorders, bone resorption diseases and endocrine hyperenergia diseases including periodontal disease, arthritis, inflammatory bowel disease, myocarditis, spinal disorders, hepatitis C, liver cirrhosis, diabetes, reperfusion disorders, disseminated intravascular coagulation, Alzheimer's disease.

No.	Publication Number	Title	Use
15	WO 2001040204	**New 1,3,4-oxadiazole derivatives are cysteine protease inhibitors for treating e.g. inflammatory, autoimmune, circulatory, neurodegenerative and pulmonary disorders.**	inhibition of cathepsin for treating inflammatory diseases, diseases induced by apoptosis, diseases induced by immune response failure, autoimmune diseases, diseases induced by the degradation of biological constituting proteins, shock, circulatory disorders, blood coagulation system disorders, malignant tumor, AIDS AIDS-related complex, parasitosis, neurodegenerative diseases, pulmonary disorders, bone resorption diseases and endocrine hyperenergia diseases including periodontal disease, arthritis, inflammatory bowel disease, myocarditis, spinal disorders, hepatitis C, liver cirrhosis, diabetes, reperfusion disorders.
16	WO 2001041815	**Inhibiting metastasis in humans by administering an agent which inhibits activity of genes which function in regulation of tumor cell metastasis, particularly genes which alter actin-based cytoskeleton of tumor cells.**	inhibition of cathepsin for treating metastatic conditions, such as melanoma, breast, ovarian, prostate, lung, bone, throat, brain, testicular, liver, stomach, pancreatic cancer or their combinations.

No.	Publication Number	Title	Use
17	WO 2001019816	New heterocyclic amide and thioamide compounds are reversible cysteine protease inhibitors used for treating e.g. rheumatoid arthritis, Alzheimer's disease, atherosclerosis and osteoporosis.	inhibition of cathepsin for treating autoimmune disease, rheumatoid arthritis, systemic lupus erythematosus, Crohn's disease, ulcerative colitis, multiple sclerosis, Guillain-Barre syndrome, psoriasis, Grave's disease, myasthenia gravis, scleroderma, glomerulonephritis, atopic dermatitis, insulin dependent diabetes mellitus, Alzheimer's disease, atherosclerosis, osteoporosis and asthma.
18	WO 2001030370	Treatment of vascular disease associated with cystatin C deficiency, including atherosclerosis, aneurismal aortic lesions, myocardial infarction and unstable angina pectoris, comprises administration of a cysteine protease inhibitor.	inhibition of cathepsin for treating and preventing development of vascular diseases, including atherosclerosis, aneurismal aortic lesions, myocardial infarction, unstable angina pectoris, abdominal aortic aneurysm and tumor-induced vascular lesions.
19	WO 2001019808	New benzyl-sulfonyl derivatives are cathepsin S inhibitors useful for treating e.g. autoimmune disorders (including juvenile onset diabetes, multiple sclerosis, pemphigus vulgaris, Graves' disease and myasthenia gravis.	inhibition of cathepsin for treating autoimmune disorders (including juvenile onset diabetes, multiple sclerosis, pemphigus vulgaris, Graves' disease, myasthenia gravis, system lupus erythematosus, rheumatoid arthritis, Hashimoto's thyroiditis), allergic disorders (including asthma), allogeneic immune responses (including organ transplants or tissue grafts), disorders involving excessive elastolysis (including chronic obstructive pulmonary disease, emphysema, bronchitis, pneumonities and cardiovascular disease) and system amyloidosis.

No.	Publication Number	Title	Use
20	WO 9958153	**Modulating autoimmunity in a subject using an agent which modulates cathepsin S activity, used for e.g. treating autoimmune disorders such as asthma.**	inhibition of cathepsin for treating autoimmune disorders such as asthma, increasing autoimmunity, or diagnosing susceptibility to an autoimmune disorder.
21	WO 9819671	**Ameliorating bone resorption disorder symptom(s), e.g. osteoporosis - by contacting inhibitor of cathepsin S activity to osteoclast to inhibit cathepsin K activity.**	inhibition of cathepsin for treating osteoporosis, arthrirides such as osteoarthritis, and periodontal disease, damage caused by macrophage-mediated inflammatory processes, or osteosclerotic disorders such as pycnodysostosis (PYCNO), lung injury associated with emphsema, and injury associated with an accumulation of macrophages at the site of atherosclerotic plaques.